Search Paper #1

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DATE: Tuesday, January 07, 2003

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
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L2	L1 same retrieval key	0	L2
L1	vector with insert	11951	L1

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1. Document ID: US 20020004242 A1

L3: Entry 1 of 4 File: PGPB Jan 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020004242
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020004242 A1

TITLE: Plasmids for construction of eukaryotic viral vectors

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McVey, Duncan L.	Derwood	MD	US	
Brough, Douglas E.	Olney	MD	US	
Kovesdi, Imre	Rockville	MD	US	

US-CL-CURRENT: 435/456; 435/320.1, 536/23.1

ABSTRACT:

The present invention provides a dual selection cassette (DSC) comprising first and second DNA segments having homology to a eukaryotic viral vector, positive and negative selection genes, each operably linked to their own promoter, and one or more unique restriction enzyme sites (URES) or sitey-directed homologous recombination sites. The present invention also provides a plasmid, pN/P, comprising an independent positive selection marker gene, an origin of replication, and a dual selection cassette. The dual selection cassette and pN/P plasmid can be used to produce eukaryotic gene transfer vectors without requiring temporally-linked double recombination events or the use of specialized bacterial strains that allow the replication of plasmids comprising defective origins of replication. This method usefully increases the ratio of desired to undesired plasmid and vector constructs. Additionally, this invention provides a method for the creation of eukaryotic viral vector libraries.

L3: Entry 1 of 4 File: PGPB Jan 10, 2002

DOCUMENT-IDENTIFIER: US 20020004242 A1
TITLE: Plasmids for construction of eukaryotic viral vectors

Detail Description Paragraph (63):
[0078] It will be appreciated that portions of the negative and (especially) the positive selection genes can constitute a portion of the first and/or second homology region. Thus, the entire dual selection cassette need not necessarily be recombined out of pN/P in the production of pDesired. Additionally, it will be appreciated that DNA segments distal to the dual selection cassette can be used as first and/or second homology regions (e.g., the ITRs of an adenovirus can serve as the first and second homology regions for homologous recombination with a pN/P plasmid comprising an adenoviral vector that further comprises a dual selection cassette in the E2A region of the adenoviral genome). In this embodiment, a eukaryotic viral replicon, wherein all viral sequences not comprising the ITRs are

eliminated from the vector by recombination with the second DNA, is created. Of course, the replicon can be created such that it also comprises a viral packaging site, such that the replicon can be packaged in a solution (in vitro) or cell (in vivo) comprising the necessary packaging components. Thus, the homologous recombination between pN/P and the second DNA also can be used to simultaneously insert sequences into a eukaryotic viral vector and form a deletion in the eukaryotic viral vector.

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2. Document ID: US 6475757 B2

L3: Entry 2 of 4 File: USPT Nov 5, 2002

US-PAT-NO: 6475757
DOCUMENT-IDENTIFIER: US 6475757 B2

TITLE: Plasmids for construction of eukaryotic viral vectors

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McVey; Duncan L.	Derwood	MD		
Brough; Douglas E.	Olney	MD		
Kovesdi; Imre	Rockville	MD		

US-CL-CURRENT: 435/91.41; 435/320.1, 435/455, 435/456, 435/463, 435/5, 435/6, 435/91.1, 435/91.4, 435/91.52

ABSTRACT:

The present invention provides a dual selection cassette (DSC) comprising first and second DNA segments having homology to a eukaryotic viral vector, positive and negative selection genes, each operably linked to their own promoter, and one or more unique restriction enzyme sites (URES) or sitey-directed homologous recombination sites. The present invention also provides a plasmid, pN/P, comprising an independent positive selection marker gene, an origin of replication, and a dual selection cassette. The dual selection cassette and pN/P plasmid can be used to produce eukaryotic gene transfer vectors without requiring temporally-linked double recombination events or the use of specialized bacterial strains that allow the replication of plasmids comprising defective origins of replication. This method usefully increases the ratio of desired to undesired plasmid and vector constructs. Additionally, this invention provides a method for the creation of eukaryotic viral vector libraries.

11 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

L3: Entry 2 of 4 File: USPT Nov 5, 2002

DOCUMENT-IDENTIFIER: US 6475757 B2
TITLE: Plasmids for construction of eukaryotic viral vectors

Detailed Description Text (63):
It will be appreciated that portions of the negative and (especially) the positive selection genes can constitute a portion of the first and/or second homology region.

Thus, the entire dual selection cassette need not necessarily be recombined out of pN/P in the production of pDesired. Additionally, it will be appreciated that DNA segments distal to the dual selection cassette can be used as first and/or second homology regions (e.g., the ITRs of an adenovirus can serve as the first and second homology regions for homologous recombination with a pN/P plasmid comprising an adenoviral vector that further comprises a dual selection cassette in the E2A region of the adenoviral genome). In this embodiment, a eukaryotic viral replicon, wherein all viral sequences not comprising the ITRs are eliminated from the vector by recombination with the second DNA, is created. Of course, the replicon can be created such that it also comprises a viral packaging site, such that the replicon can be packaged in a solution (in vitro) or cell (in vivo) comprising the necessary packaging components. Thus, the homologous recombination between pN/P and the second DNA also can be used to simultaneously insert sequences into a eukaryotic viral vector and form a deletion in the eukaryotic viral vector.

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3. Document ID: US 6458592 B1

L3: Entry 3 of 4 File: USPT Oct 1, 2002

US-PAT-NO: 6458592
DOCUMENT-IDENTIFIER: US 6458592 B1

TITLE: Production of antibodies using cre-mediated site-specific recombination

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jakobovits; Aya	Menlo Park	CA		
Zsebo; Krisztina M.	Woodside	CA		

US-CL-CURRENT: 435/455; 435/320.1, 435/325, 435/326, 435/69.1, 435/69.7, 435/70.1, 435/70.21, 800/13, 800/18

ABSTRACT:

A method to produce a cell expressing an antibody from a genomic sequence of the cell comprising a modified immunoglobulin locus using Cre-mediated site-specific recombination is disclosed. The method involves first transfecting an antibody-producing cell with a homology-targeting vector comprising a lox site and a targeting sequence homologous to a first DNA sequence adjacent to the region of the immunoglobulin loci of the genomic sequence which is to be converted to a modified region, so the first lox site is inserted into the genomic sequence via site-specific homologous recombination. Then the cell is transfected with a lox-targeting vector comprising a second lox site suitable for Cre-mediated recombination with the integrated lox site and a modifying sequence to convert the region of the immunoglobulin loci to the modified region. This conversion is performed by interacting the lox sites with Cre in vivo, so that the modifying sequence inserts into the genomic sequence via Cre-mediated site-specific recombination of the lox sites. Also disclosed are a form of the method used to produce a cell expressing a modified antibody molecule using Cre-mediated site-specific recombination, and antibody-producing cells obtainable by the disclosed methods. Class-switching modifications of human antibodies produced in murine hybridoma cells are exemplified.

22 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

L3: Entry 3 of 4 File: USPT Oct 1, 2002

DOCUMENT-IDENTIFIER: US 6458592 B1
TITLE: Production of antibodies using cre-mediated site-specific recombination

CLAIMS:

3. The method of claim 1 further comprising an additional step before step (b) which additional step comprises transfecting said cell in vitro with a second homology-targeting vector comprising: (i) a third lox site suitable for Cre-mediated recombination with said first and second lox sites, (ii) a first selectable marker gene operably linked to control regions such that said first marker gene is expressed in said cell, and (iii) a targeting sequence homologous to a second DNA sequence adjacent said region of the immunoglobulin locus, said region being flanked by said first and second DNA sequences, so that said third lox site and said first marker gene are inserted into said immunoglobulin locus via site-specific homologous recombination with genomic DNA in vitro; and wherein in step (b), said lox-targeting vector further comprises a second selectable marker gene operably linked to control regions such that said second marker gene is expressed in said cell, so that in step (c), on interacting the lox sites with Cre, said second marker gene and said modifying sequence insert into said immunoglobulin locus via Cre-mediated site-specific recombination of said lox sites; and in step (d), said selecting for a transfectant comprises selecting for a transfectant expressing said second marker gene.

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4. Document ID: US 6329200 B1

L3: Entry 4 of 4 File: USPT Dec 11, 2001

US-PAT-NO: 6329200
DOCUMENT-IDENTIFIER: US 6329200 B1

TITLE: Plasmids for construction of eukaryotic viral vectors

DATE-ISSUED: December 11, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McVey; Duncan L.	Derwood	MD		
Brough; Douglas E.	Olney	MD		
Kovesdi; Imre	Rockville	MD		

US-CL-CURRENT: 435/320.1; 435/91.4, 435/91.41, 435/91.42, 536/23.1, 536/24.1

ABSTRACT:

The present invention provides a dual selection cassette (DSC) comprising first and second DNA segments having homology to a eukaryotic viral vector, positive and negative selection genes, each operably linked to their own promoter, and one or more unique restriction enzyme sites (URES) or site-directed homologous recombination sites. The present invention also provides a plasmid, pN/P, comprising an independent positive selection marker gene, an origin of replication, and a dual selection cassette. The dual selection cassette and pN/P plasmid can be used to

produce eukaryotic gene transfer vectors without requiring temporally-linked double recombination events or the use of specialized bacterial strains that allow the replication of plasmids comprising defective origins of replication. This method usefully increases the ratio of desired to undesired plasmid and vector constructs. Additionally, this invention provides a method for the creation of eukaryotic viral vector libraries.

26 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

L3: Entry 4 of 4 File: USPT Dec 11, 2001

DOCUMENT-IDENTIFIER: US 6329200 B1
TITLE: Plasmids for construction of eukaryotic viral vectors

Detailed Description Text (66):
It will be appreciated that portions of the negative and (especially) the positive selection genes can constitute a portion of the first and/or second homology region. Thus, the entire dual selection cassette need not necessarily be recombined out of pN/P in the production of pDesired. Additionally, it will be appreciated that DNA segments distal to the dual selection cassette can be used as first and/or second homology regions (e.g., the ITRs of an adenovirus can serve as the first and second homology regions for homologous recombination with a pN/P plasmid comprising an adenoviral vector that further comprises a dual selection cassette in the E2A region of the adenoviral genome). In this embodiment, a eukaryotic viral replicon, wherein all viral sequences not comprising the ITRs are eliminated from the vector by recombination with the second DNA, is created. Of course, the replicon can be created such that it also comprises a viral packaging site, such that the replicon can be packaged in a solution (in vitro) or cell (in vivo) comprising the necessary packaging components. Thus, the homologous recombination between pN/P and the second DNA also can be used to simultaneously insert sequences into a eukaryotic viral vector and form a deletion in the eukaryotic viral vector.

Term	Documents
SECOND.DWPI,EPAB,JPAB,USPT,PGPB.	4063772
SECONDS.DWPI,EPAB,JPAB,USPT,PGPB.	355230
HOMOLOGY.DWPI,EPAB,JPAB,USPT,PGPB.	30394
HOMOLOGIES.DWPI,EPAB,JPAB,USPT,PGPB.	4521
HOMOLOGYS.DWPI,EPAB,JPAB,USPT,PGPB.	1
(1 SAME (SECOND ADJ HOMOLOGY)).USPT,PGPB,JPAB,EPAB,DWPI.	4
(L1 SAME SECOND HOMOLOGY).USPT,PGPB,JPAB,EPAB,DWPI.	4

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